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חוק הפטנטים , תשכ"ז - 1967
PATENT LAW, 5727 - 1967

בקשה לפטנט
Application For Patent

לשימוש הלשכה
For Office Use

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אני, (שם המבקש, מענו ולגבי גוף מאוגד - מקום התאגדותו)
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בעל אמצאה מכח הדין Operation of Law ששמה הוא
Owner, by virtue of of an invention the title of which is

(בעברית) מתקן ושיטה לזריקה תת-עורית
(Hebrew)

(באנגלית) DEVICE AND METHOD FOR HYPODERMIC INJECTION
(English)

מבקש בזאת כי ינתן לי עליה פטנט
hereby apply for a patent to be granted to me in respect thereof

• בקשת חלוקה - Application of Division	• בקשת פטנט מוסף - Application for Patent Addition	• דרישת דין קדימה Priority Claim		
מבקשת פטנט from Application	לבקשה/לפטנט to Patent/Appl.	מספר/סימן Number/Mark	תאריך Date	מדינת האיגוד Convention Country
מס' No.	מס' No.			
מיום dated	מיום dated			

יפוי כח: כללי
P.O.A.: general/individual-attached/to be filed later-

הוגש בענין filed in case

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היום 10 בחודש Jul שנת 2002
This of of the year

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מתקן ושיטה לזריקה תת-עורית

DEVICE AND METHOD FOR HYPODERMIC INJECTION

Device and Method for Hypodermic Injection

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to hypodermic injection and, in particular, it concerns a device and method for hypodermic injection which employ a combination of shallow penetration by hollow microneedles followed by jet injection via the microneedles.

It is known to employ devices based upon hollow microneedles for transferring fluids across a biological barrier. Examples of microneedle structures, devices employing such microneedles, and production techniques therefor may be found in PCT Publications Nos. WO01/66065 and WO02/17985, both coassigned with the present application. These publications are hereby incorporated by reference as if set out in their entirety herein.

Microneedles provide a particularly advantageous mechanism for delivery of fluids through the impermeable outer layers of the skin while ensuring that penetration is sufficiently shallow that minimal discomfort is caused. This renders devices based upon microneedles safe for self-administered medications and offers a much more effective alternative to the conventional transdermal drug delivery patch.

Since, however, microneedles typically penetrate only into the layers of the lower epidermis or dermis, flow rates for introducing drugs are highly limited and the time taken for diffusion of a drug into the vascular system and thus around the body is relatively long. As such, current microneedle-based

devices are not generally considered suitable for applications where immediate delivery of a drug into the vascular system is required, or where the injection of a significant quantity of a drug must be performed in a short time, such as for mass immunizations.

It is also known to employ a needleless injector as an alternative to a hollow needle for injection of fluid into the body. These injectors use a fine stream or "jet" of pressurized liquid to penetrate the skin. Pain is considerably less than that experienced during a conventional injection. Early designs used high pressure throughout the injection, to punch a hole through the tough epidermis. However, the bulk of the injection could then be infused along the initial track under much lower pressure. U.S. Pat. No. 2,704,542 to Scherer and U.S. Pat. No. 3,908,651 to Fudge disclose examples of this design. Ultimately, the engineering demands of changing the pressure during the injection and resulting complexity have limited the use of such devices.

In most cases, modern high-pressure needleless jet injectors are driven by pressure from a pressurized gas cylinder as exemplified by U.S. Patents Nos. 6,063,053 and 6,264,629. U.S. Patent No. 5,499,972 teaches a jet injection device powered by a powerful cocked spring. Of most relevance to the present invention are U.S. Patents Nos. 6,102,896 and 6,224,567 which teach a jet injection device where the pressure is generated manually by pressing on a cap. When sufficient force is applied, a mechanical obstruction is overcome to actuate the pressure jet.

While jet injectors offer advantages of reduced pain and improved hygiene compared to conventional needle injections, they still suffer from many drawbacks. Most notably, since there is no sealed conduit between the drug supply and the target tissue, significant wastage of the drug occurs. This also results in lack of precision in the administered dosage of a drug. Furthermore, penetration through the strong tissue of the upper layers of the skin requires high activation pressures which typically require complex and expensive systems. The use of purely manual pressure for activation may raise questions of reliability.

There is therefore a need for a device and method which would achieve relatively painless shallow penetration by use of hollow microneedles followed by jet injection via the microneedles.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is a device and method for hypodermic injection which employ a combination of shallow penetration by hollow microneedles followed by jet injection via the microneedles.

The principles and operation of devices and methods according to the present invention may be better understood with reference to the drawings and the accompanying description.

Referring now to the drawings, Figures 1-4 illustrate four variant preferred implementations of a device constructed and operative according to the teachings of the present invention. Generally speaking the devices include a

cylinder housing a quantity of a liquid composition to be injected and a microneedle interface including at least one, and preferably a two-dimensional array of, hollow microneedles. A hand-operated cover is manually depressible so as to apply force to a piston which forces the liquid through the hollow microneedles to form fine jets therefrom.

It is a particular feature of the present invention that the device is configured to prevent initial flow of the liquid through the microneedles until the applied manual pressure is sufficient to ensure a resultant fluid pressure, at least momentarily, of at least about 1000 pounds per square inch (psi). Most preferably, this is achieved by placing an appropriately designed breakable membrane or "diaphragm" between the initial location of the liquid and the microneedles. The diaphragm is designed, typically with lines of reduced thickness or strength, to fracture within a predefined range of applied pressure. The range is typically chosen to be between about 1000 and about 1500 PSI. This structure also ensures that the liquid cannot escape prematurely from the microneedles and is sealed from the atmosphere prior to use.

The liquid may be either loaded directly into the cylinder (Figures 2 and 4) or located in a capsule or cartridge (Figures 1 and 3). In either case, a priming or mixing action may be performed shortly prior to, or during, the initial application of pressure to the piston.

The manual application force may be used to displace a relatively stiff or "rigid" cover so as to snap into an activated position in which slight elastic deformation of the cover maintains a roughly constant force on the piston. This

option may readily be implemented using molded plastic components. Example of this type of implementation are shown in Figures 1 and 2.

A second option, shown in Figures 3 and 4, is the use of a more flexible cover made, for example, from synthetic rubber or the like. In this case, manually applied pressure is transferred directly to the piston.

As in the prior PCT publications incorporated by reference above, the definition of the term "microneedle" in this context is taken to be a needle of length (or "height" as viewed standing from the surface of a substrate) of less than 2 mm. Preferably, the height is no more than 0.6 mm, and most preferably in the range 0.4-0.6 mm. This ensures that the tough outer layers of the skin are penetrated mechanically prior to actuation of the liquid jet, while still minimizing discomfort.

The bore of the hollow microneedles, and the resulting output liquid jet, preferably has a diameter of between about 0.05 mm - 0.07mm. Other dimensions and spacing of the microneedles are preferably as described in the aforementioned PCT publications, although other values may be used according to the requirements of a given application.

The preferred diameter of the piston-cylinder configuration generating the jet pressure is no more than about 2 mm, and preferably between 1 and 2 mm. It will be appreciated that manual application of about 3 kg force to this area generates between about 100 and about 400 kg per square cm (about 1400 to about 5600 psi). Typically, lower pressure is required for a given depth of

penetration compared to conventional jet injection techniques due to the initial penetration of the hard outer skin layers by the microneedles.

As a result of the channel formed by penetration of the liquid jet into the subcutaneous tissue and the high speed delivery pulse, the total delivery time is typically less than a second for a delivered volume of 1-2 micro-liters (cubic millimeters).

Turning briefly to the breakable membrane or diaphragm, this is based on a concept commonly used in many mechanical systems such as safety devices in various high pressure systems. The diaphragm may be implemented as a sphere with accurate thickness; a layer or film with accurate thickness; or as a layer or film with accurate thickness and in addition weakened at the center by making mark or pattern. The option of a predefined breaking pattern may have advantages for ensuring that the remnants do not form any blockage of flow through the device.

Finally, the operation of the device of the present invention and the corresponding broad method will now be clearly understood. The method in its broadest sense may be regarded simply as the steps of: (a) penetrating outer layers of skin to a depth of less than 2 mm, and preferably less than 0.6 mm, with at least one hollow microneedle; and (b) generating a flow of liquid through the bore(s) of the microneedle(s) with sufficient speed to achieve jet injection through tissue beyond the depth of penetration of the microneedle(s). The energy for the flow is preferably provided exclusively by manually applied

force. The preferred parameters of the device used to implement the method are the preferred parameters of the device as described above.

It will be appreciated that the above descriptions are intended only to serve as examples, and that many other embodiments are possible within the scope of the present invention.

WHAT IS CLAIMED IS:

1. A device for injecting a liquid into a body substantially according to any feature or combination of features described above.

2. A method for injecting a liquid into a body substantially according to any feature or combination of features described above.

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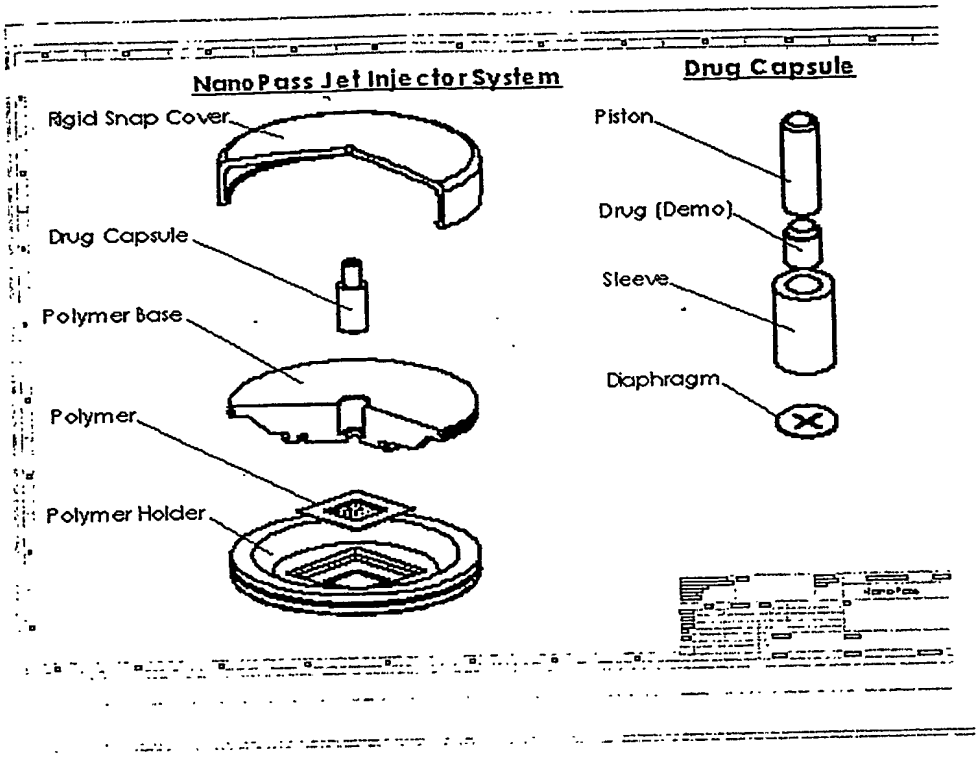
Figure 1: Jet system with snap cover and drug capsule



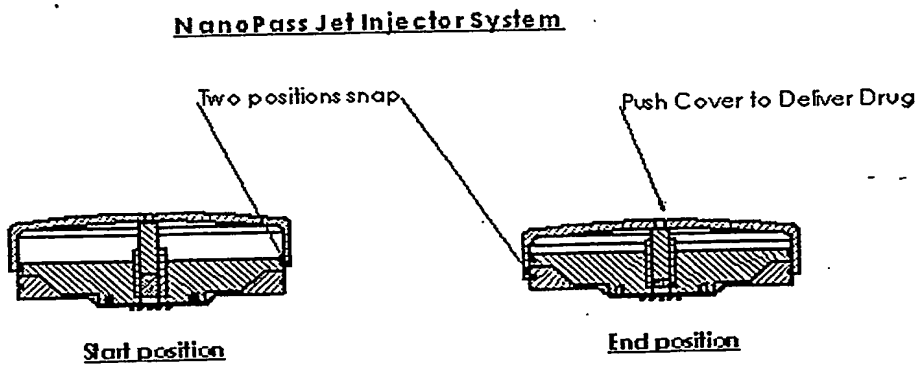
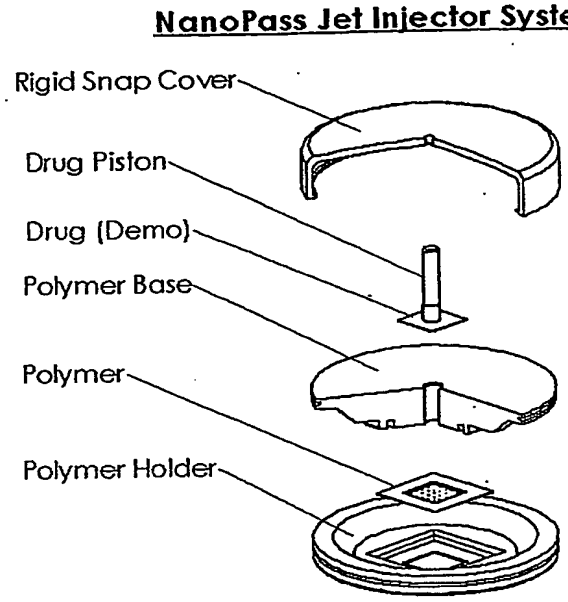
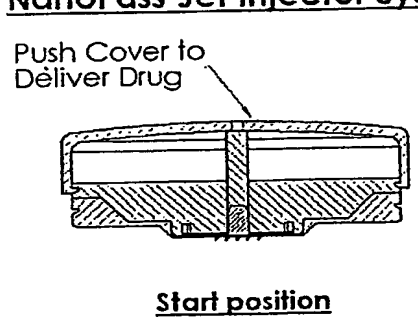


Figure 2: Jet system with snap cover and drug in barrel





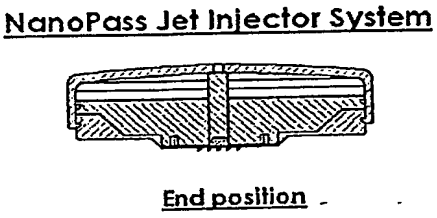


Figure 3: Jet system with rubber cover and drug capsule

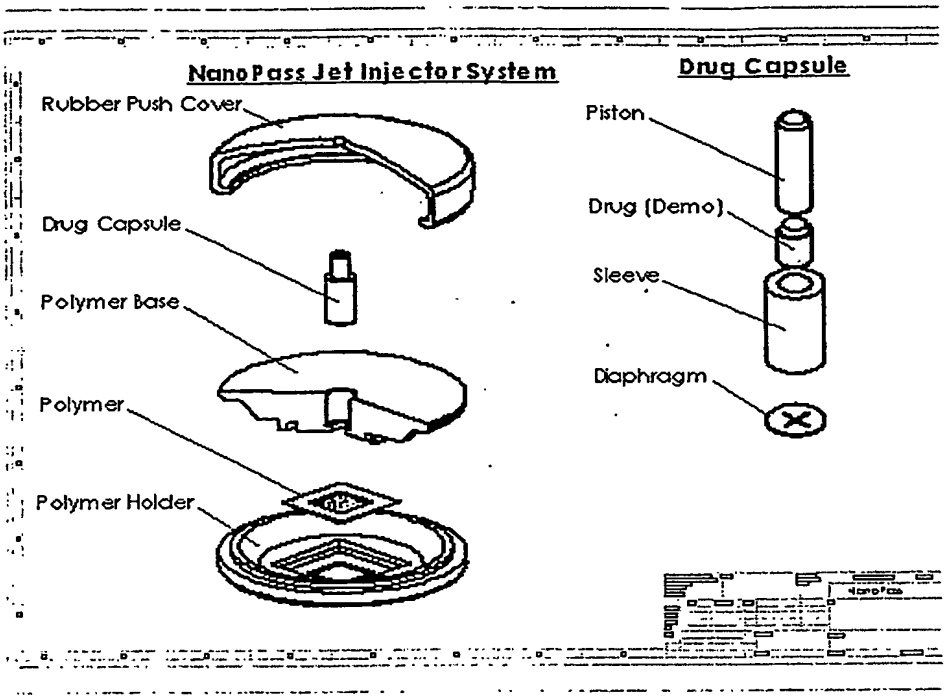
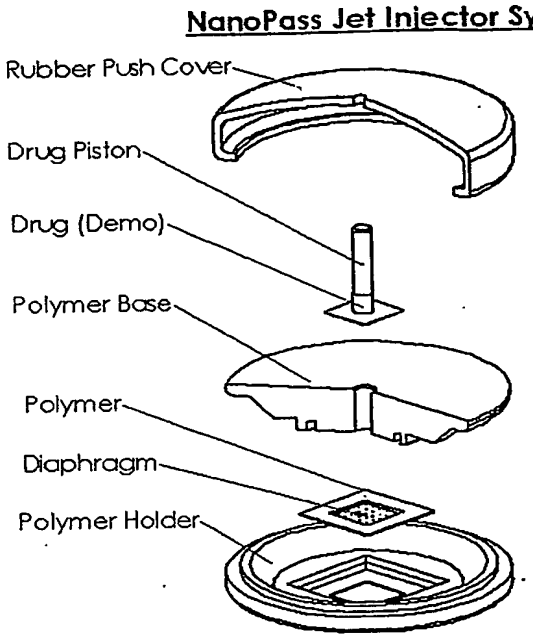
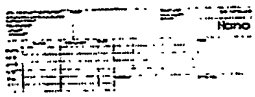
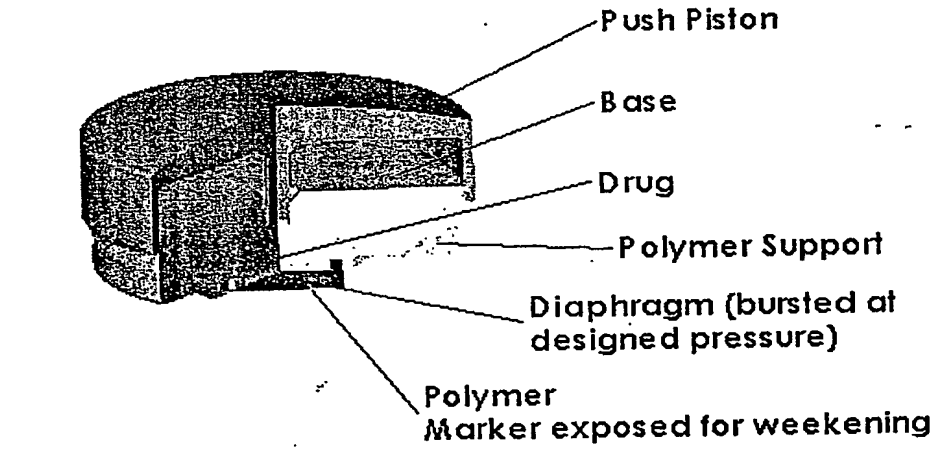


Figure 4: Jet system with rubber cover and drug in barrel







Nano Patch - Jet Injection Chip

End Position - Drug under pressure